DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration
Seattle District
Pacific Region
22201 23rd Drive SE
Bothell, WA 98021-4421

Telephone: 425-486-8788
FAX: 425-483-4996

March 29, 2001

VIA CERTIFIED MAIL
RETURN RECEIPT REQUESTED

In reply refer to Warning Letter SEA 01-42

Barry Plost, Chief Executive Officer
SeraCare, Inc.
1925 Century Park East, Suite 1970
Los Angeles, California 90067

WARNING LETTER

Dear Mr. Plost:

We inspected your firm located at 2802 Hoyt Avenue, Everett, Washington, on February 5, 6, 7, 8, 9, 12, and 14, 2001. During that inspection our investigators documented violations of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act and Title 21, Code of Federal Regulations (21 CFR), Parts 600-680 as follows:

1. Failure to maintain and/or follow written standard operating procedures (SOPs) to include all steps to be followed in the collection, processing, testing, storage, and distribution of blood and blood components [21 CFR 606.100(b)] in that:

   a) Donor [redacted] experienced a reaction on January 17, 2001 that began with slow speech, blurry vision, and weak breathing. SeraCare SOP 50.1, Hypotensive/VasoVagal Reactions Automated, requires the center physician/physician substitute to be notified if a reaction reaches the level of blurry vision. No contact was made. During the reaction the donor experienced loss of consciousness for 2-3 seconds, irregular pulse, and a blood pressure of 66/30. A call to 911 was placed 40 minutes after the onset of the reaction.

   b) The SeraCare Physician Substitute Reference Manual, which also includes procedures for the supervising, licensed, physician, was not followed in that the licensed physician failed to review random charts on a weekly basis. The reference manual states that the supervising, licensed physician must review random charts for donors attended by the physician substitute as evaluation and review of the physician substitute's performance of their duties. The Physician Substitute Log, the log utilized to document the review,

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   b) The SeraCare Physician Substitute Reference Manual, which also includes procedures for the supervising, licensed, physician, was not followed in that the licensed physician failed to review random charts on a weekly basis. The reference manual states that the supervising, licensed physician must review random charts for donors attended by the physician substitute as evaluation and review of the physician substitute's performance of their duties. The Physician Substitute Log, the log utilized to document the review,

includes only one date between November 7, 2000 and February 7, 2001 that the licensed physician reviewed donor charts handled by the physician substitute.

c) SeraCare SOP 50.10, Donor Medical Incident Report, requires the licensed physician to review all Medical Incident Reports to determine donor eligibility for continued donation, document an impression or diagnosis of what the probable cause of the reaction was, and determine what type of reaction occurred. Four of nine Medical Incident Reports prepared since November 7, 2000, when SeraCare assumed ownership of this facility, have not been reviewed by the licensed physician, including Medical Incident Reports for Donor [redacted], dated November 15, 2000; Donor [redacted], dated January 2, 2001; Donor [redacted], dated January 17, 2001; and Donor [redacted], dated January 24, 2001. Two of these donors [redacted] and [redacted] were permitted to donate following the adverse donor reactions without a determination made by the licensed physician for continued eligibility.

d) Donor [redacted] was not deferred for eight weeks following two blood losses of less than 200 ml, as required by SeraCare SOP 30.12, RBC Losses. Donor [redacted] experienced blood losses on October 20, 2000 and November 17, 2000, but was permitted to donate fifteen times over the next eight weeks.

2. Failure to assure that personnel have the training and experience necessary for the competent performance of their assigned functions [21 CFR 606.20(b)] in that:

a) Employees did not competently calculate deferral periods for seven donors in accordance with SeraCare SOP 30.12. Donors deferred for red blood cell losses had deferral periods calculated at less than eight weeks (Donors [redacted] and [redacted]). Our investigator was advised during the inspection that center personnel were trained to calculate deferral periods incorrectly.

b) Lookbacks to identify unsuitable units collected from donors with sexual partners testing reactive for anti-HCV were not performed for Donors [redacted] (no donor number) and [redacted] as required by SeraCare SOP 60.7, Receipt of Unsuitable Test Results. The Facility Director, Roke M. Murillo, acknowledged that he did not know a lookback was required in these situations.

The above identified deviations are not intended to be an all inclusive list of deficiencies at your facility. It is your responsibility to assure that your establishment is in compliance with all requirements of the federal regulations.

We acknowledge receipt of a response letter from Claus L. Winther, President/Authorized Official, Biologics Division, dated February 21, 2001. The letter addresses the inspectional observations listed on Form FDA 483 issued at the close of the inspection. The response letter

did not provide sufficient detail to address the adequacy of the corrective actions. Our evaluation of the response letter is detailed below. Our comments are numbered to correspond to the numbering system on the Form FDA 483.

I.a.1.i., ii	Documentation of retraining, including the content of the training session, was not provided for review, therefore, could not be evaluated for adequacy.
I.a.2.i., ii., iii., iv., v., I.a.3.	Documentation of retraining, including the content of the training session, was not provided for review, therefore, could not be evaluated for adequacy. In addition, you have not indicated whether the deficiencies with documentation for this medical incident will be corrected.
I.b. I.c.1.,2.,3.	Documentation of retraining, including the content of the training session, was not provided for review, therefore, could not be evaluated for adequacy.
I.d.	This inspectional observation states that SOP 50.10 is inadequate in that it "does not address how to track, route and file the report to ensure the completion of the form and determine the donor's continued suitability to donate." Nine Medical Incident Reports were provided for review during the inspection, of which the licensed physician had not reviewed four. When center staff was questioned by the investigator about the failure of the licensed physician to review these forms, he was told that the forms are either placed in the donor record file and then into the physician's office, or the staff writes a note to the physician. Neither of these practices are addressed in the SOP and, based on the number of reports that had not been reviewed, it appears the practice is not adequate to ensure review will occur. We request that you re-evaluate your disagreement with this observation and consider implementing corrective action to assure Medical Incident Reports are reviewed by the licensed physician in a timely manner. In addition, the ultimate filing of the report should be addressed in the SOP and should ensure that all Medical Incident Reports will be available for review during an inspection.
I.e.	Your correction to this item, failure to post emergency telephone numbers near telephones, is adequate and was verified during the inspection.
II.	Documentation of retraining the licensed physician, including the content of the training session, was not provided for review, therefore, could not be evaluated for adequacy. Documentation of the licensed physician's retroactive review of required records was not provided for review, therefore, could not be evaluated for adequacy.

III This corrective action could not be verified as the documentation of staff member CPR certification would not be available until the course is completed, which is scheduled for a future date.

IV.a., b., c. Documentation of retraining, including the content of the training session, was not provided for review, therefore, could not be evaluated for adequacy. The inspection identified seven donor records that included a miscalculation of donor deferral times that shortened the deferral time. You should consider conducting a retroactive review of donor records to identify any additional discrepancies with the application of deferral time periods.

V.a.1. V.a.3. In your response letter you state that Post Donation Information Reports are to be used when events occurring prior to the donation were not revealed, but were later ascertained. SOP 40.4 states that post donation information is any information obtained after a donation which, if known, may or may not have caused the donor to be deferred. You specifically list exposure to Hepatitis and unsuitable sexual practices as two examples. We are unsure as to why you feel this information would not be categorized in the above. SOP 40.4 indicates that completion of the Post Donation Information Report, and subsequent investigation, can prompt the completion of a Lookback Alert Notification. For this donor, you failed to complete the lookback as required by SeraCare SOP 60.7. FDA's Guidance Regarding Post Donation Information Reports, dated December 10, 1993 (copy enclosed), addresses the documentation of post donation information to ensure the timely investigation of information to determine if the safety, purity, or potency of blood and blood components may have been affected. Written Standard Operating Procedures, 21 CFR 100(b), are to be maintained and followed for the collection, processing, testing, storage, and distributing of blood and blood components. We consider your response to this inspectional observation to be inadequate in that you do not address a corrective action. Your corrective action should also address the process that led to your failure to conduct a lookback.

V.a.2. For the same reasons listed above, we believe that post donation information related to incarceration should prompt the completion of a Post Donation Information Report. Your response states that the donor did not donate after his incarceration or after you were informed of his incarceration. You also again use the definition of post donation information as "events occurring prior to the donation were not revealed, but were later ascertained". Based on the above information it appears that you may have conducted a limited investigation into this post donation information, but did not complete the required form. You have indicated that you evaluated the timeframe for the incarceration and its relationship to donated Source Plasma, therefore, this investigation should have been appropriately documented on a Post Donation Information Report. We

consider your response to this inspectional observation inadequate in that you failed to provide a corrective action.

V.b.1. See our response under V.a.1. above. We consider your response to this inspectional observation inadequate in that you failed to provide a corrective action.

V.b.2. Documentation of retraining, including the content of the training session, was not provided for review, therefore, could not be evaluated for adequacy. In addition, your corrective action should address the process that led to your failure to conduct a lookback.

V.c. Documentation of retraining, including the content of the training session, was not provided for review, therefore, could not be evaluated for adequacy.

VI. Documentation of "delayed entries" on SPE reports were not provided for review, therefore, could not be evaluated for adequacy. An example of the new laboratory form was not provided, therefore, we could not address whether SOP 20.31, Physician/Physician Substitute Record Review, would now be adequate.

VII.a. Documentation of retraining, including the content of the training session, and the repair log were not provided for review, therefore, could not be evaluated for adequacy.

VII.b. The inspectional observation states that quarterly calibration and standardization for the [redacted] Instrument were performed after the daily controls were tested. Your [redacted] Control Log documents that the quality control check was performed prior to bringing the instrument back into service, but staff failed to perform the quarterly timer calibration as required by SOP 70.2. SOP 70.2 states that all required standardization/calibration and quality control must be recorded prior to bringing the instrument back into service. The observation states that center management was aware of the discrepancy, documented the discrepancy, but did not run the controls again until after additional donors were tested. Your procedure requires both to be performed prior to placing equipment back into service. Therefore, your response is inadequate in that you did not address a corrective action for failure to perform both prior to putting the instrument back into service. The later performance of the part of the standardization that was missed does not appear to be adequate in that your procedure requires all parts to be performed at the same time, prior to a return to service. The inspectional observation does not cite the failure to identify which should be ran first, although that was discussed during the inspection. The failure of the written procedure to address the order in which the calibration and the quality control check should be

performed should be addressed after determination of the equipment manufacturer's requirements.

VII.c. Your correction to this item, obliteration of quality control lot number and expiration date information, is adequate and was verified during the inspection.

VIII. The inspectional observation states that SOP 20.19, Vital Sign Determination, is inadequate in that there are no instructions for responding to display messages, including documentation and reporting the messages at your center. Neither the procedure, nor the operator's manual, includes guidance for employees on how to document display messages, and whether a display message requires a repeat vital sign determination. You are responsible for developing adequate standard operating procedures to guide your employees in all steps to be followed in the collection, processing, testing, storage, and distribution of blood and blood components [21 CFR 606.100(b)]. An employee that obtained a display message on the vital sign instrument was observed to lack knowledge in how to respond to the message. Your response is inadequate in that you do not provide a corrective action that addresses how your staff will respond to display messages, whether it be an error message or an advisory message, how they will document the messages, and whether or not the vital sign determination must be repeated. In addition, we could not locate the "simple troubleshooting exercise" you referred to in your response.

IX. Documentation of retraining, including the content of the training session, the "internal system that will assure future compliance", and the corrected Unsuitable Products Checklist were not provided for review, therefore, could not be evaluated for adequacy.

X. During the inspection our investigators were advised that if a donor was not currently on a medication, the donor question asking about recent medications was to be checked "No". You state the donor had not taken the medication for over one week, therefore the question was appropriately marked "No". You also state that you have now documented the investigation in the Donor Record File. You did not provide the Donor Record File for review, therefore we could not evaluate for adequacy.

You should take prompt measures to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Such action includes license suspension and/or revocation, seizure, and/or injunction.

Please notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations and to prevent their recurrence. If corrective

action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Your reply should be sent to the Food and Drug Administration, 22201 23rd Drive SE, Bothell, Washington 98021-4421, Attention: Lisa M. Althar, Compliance Officer.

We acknowledge your request to discuss this inspection. After receipt of this letter, if you still wish to discuss, please contact Compliance Officer Lisa Althar at this office to arrange a date and time.

Sincerely,

for Charles M. Breen
District Director

Enclosures:
Form FDA 483
FDA's Guidance Regarding Post Donation Information Reports, dated December 10, 1993

cc: Claus L. Winther, President/Authorized Official
Biologics Division
SeraCare, Inc.
919 West Cucharras
Colorado Springs, Colorado 80905

Mr. Roke M. Murillo, Facility Director
SeraCare Acquisitions, Inc.
2802 Hoyt Avenue
Everett, Washington 98201